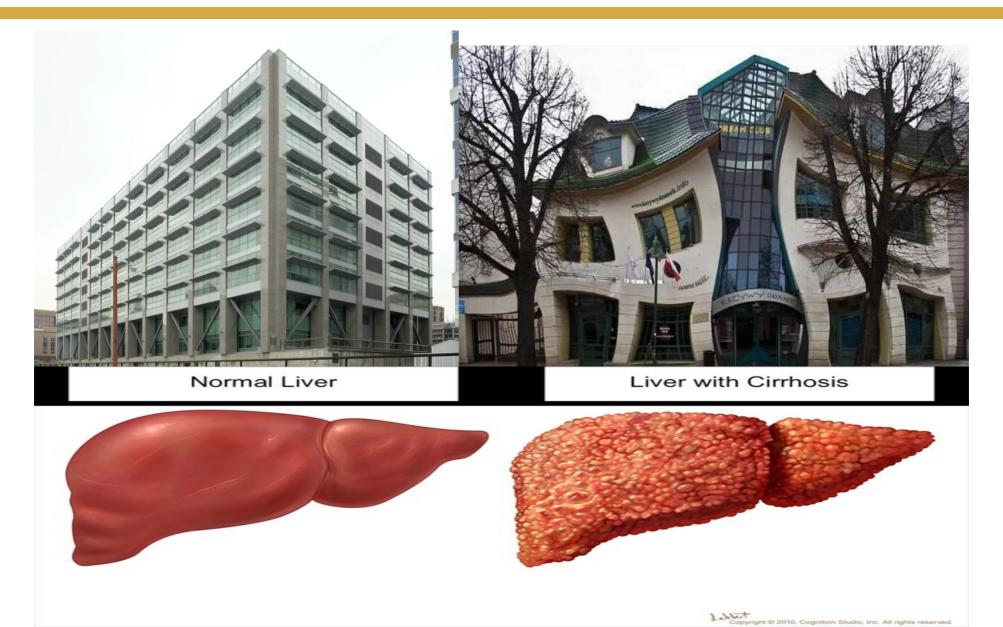




Dr. Riham Abu-Zeid Prof. of Pathology

Dr. Nagwa Ramadan Ahmed Professor of Internal Medicine *Cairo - University* 





#### **INTENDED LEARNING OBJECTIVES (ILO)**



- Classify cirrhosis
- Explain pathogenesis and complications of cirrhosis and portal hypertension
- Determine symptoms & signs of liver cirrhosis
- Correlate pathologic features of cirrhosis with the clinical picture, investigations and complications
- Approach diagnosis of liver cirrhosis
- Plan for management of liver cirrhosis

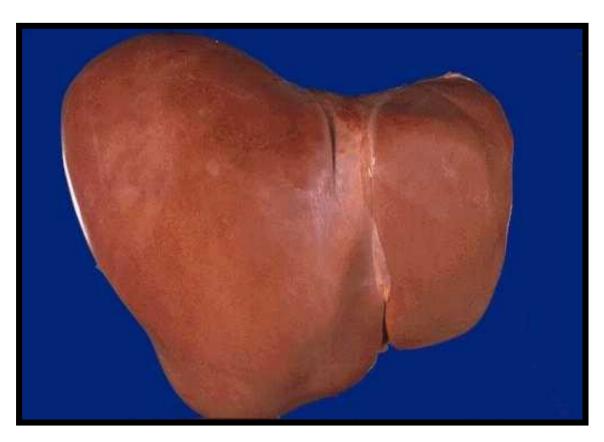


# Definition

- Chronic progressive diffuse liver disease
- •Characterized by <u>conversion of normal hepatic</u> <u>architecture into structurally abnormal nodules by</u> <u>fibrosis</u>
- End result of chronic liver disorders

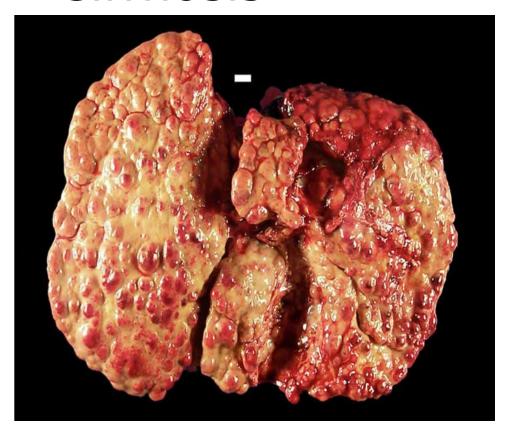


# Normal Liver



https://webpath.med.utah.edu/jpeg4/LIVER002.jpg

# Cirrhosis

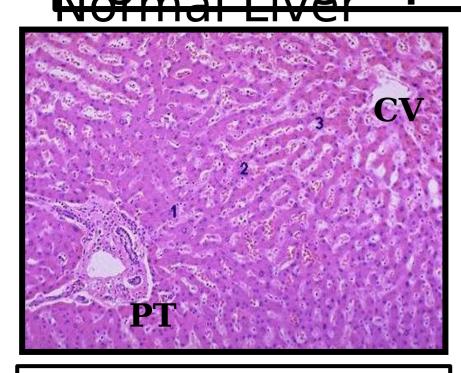


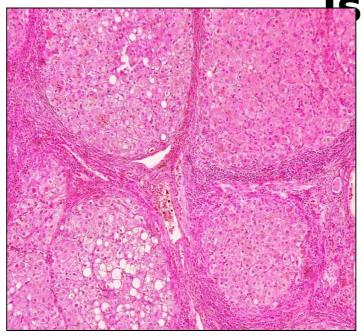
https://3.imimg.com/data3/TP/XL/MY-2297891/hydatid-cysts-of-the-liver-125x125.jpg

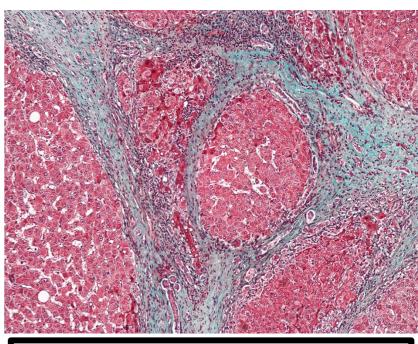
Gross: Nodular outer and cut section
Nodules surrounded by fibrous



=Fibrous septa + Parenchymal nodules of Cirrhos regenerating hepatocytes







Collagen in liver capsule portal tracts around centraled. Vielnshipeg4/LIVER003.jpg

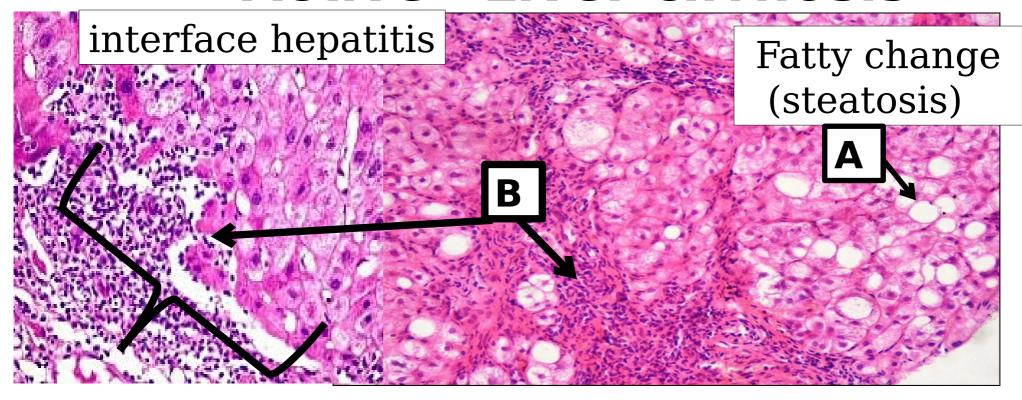
**Nodules** separated by fibrous tissue Sen Ostalides ,Pathology Department ,Ain Shams University

Maisson **Trichrome stain** 

https://i.pinimg.com/originals/06/52/3a/06523a40c7ae308cb8956cb46a3cada



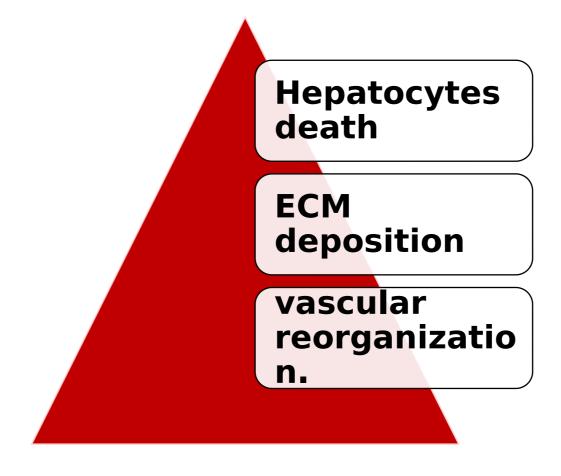
# "Active" Liver cirrhosis



Fibrous tissue >>inflammation + interface & or lobular hepatitis

# **Explain pathogenesis of Cirrhosis**

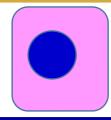


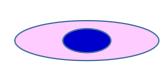


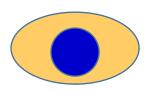
## **Explain pathogenesis of Cirrhosis**











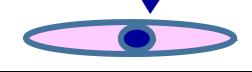
Chronic inflammatory cells

Injured Cells: hepatocytes, endothelial & Kupffer cells

Increase Cytokines & growth factors

Perisinusoidal Stellate Cells (Ito cells)





Myofibrobla



Collagen deposition & ECM

nodule formation

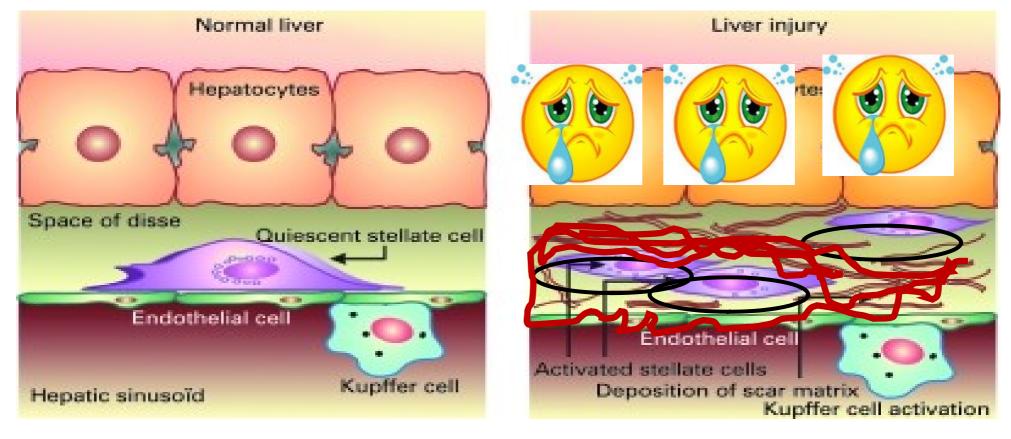
GIT & Metabolism

#### **Pathogenesis of Cirrhosis**



#### 1-Hepatocyte death

#### 2 -ECM deposition

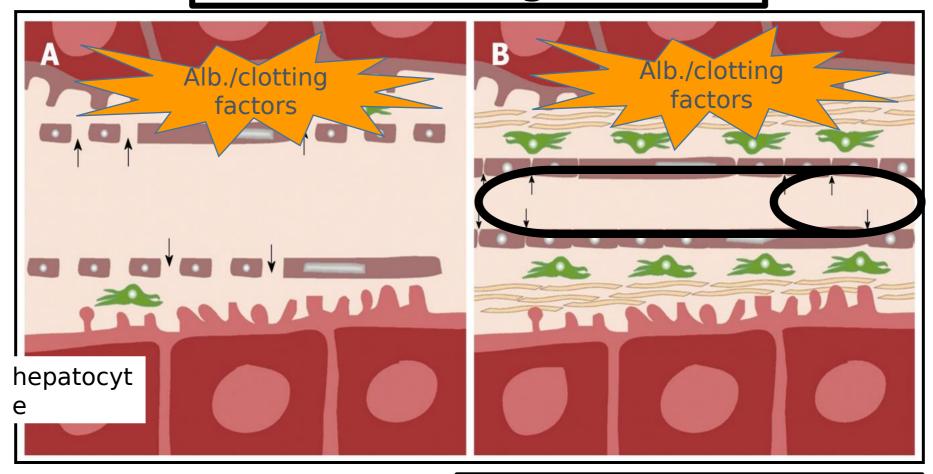


Liver injury >>activation of stellate cells >>transform into myofibroblasts >>produce collagen leading progressive fibros closure of endothelial fenestrations.

# **Pathogenesis of Cirrhosis**



#### 3-Vascular reorganization.



https://f6publishing.blob.core.windows.net/8d07584b-ca71-439b-8de5-a29fbcc57bc7/WJG-16-1598-q002.jpg

loss of sinusoidal endothelial cell

GIT & Metabolism

# Pathogenesis of Cirrhosis (Summary)



- 1. Hepatocyte death, stimulated kupffer cells, endothelial cells chronic inflammation increase production of cytokines (TNF), (IL-1),
- 2. Extracellular matrix deposition
  - Cytokines stimulate <u>perisinusoidal</u> <u>stellate</u> cells (Ito cells) to transform into a <u>myofibroblast-like</u> cell
  - Activated stellate cells (myofibroblast) stimulate collagen synthesis
  - Portal fibroblasts also participate in some forms of cirrhosis.

## Pathogenesis of Cirrhosis (Summary cont.)



#### 3. Vascular reorganization

- Collagen deposition leads to loss of sinusoidal endothelial cell fenestrations
- Conversion of sinusoids to higher pressure, fast-vascular channels without solute exchange.
- In particular, the movement of proteins (e.g., albumin, clotting factors, lipoproteins) between hepatocytes and the plasma is markedly impaired.
- High pressure in portal circulation leads to <u>development</u>
   <u>of porto-systemic vascular shunts</u>

#### Effects of cirrhosis (Quiz)



# What are the effects of cirrhosis you expect?

Impaired exchange of solutes between plasma & hepatocytes

higher sinusoidal & portal pressure

#### Pathogenesis of cirrhosis (Quiz)



Name the cell responsible for collagen deposition in cirrhosis

Ito cell



#### **Classification of Cirrhosis**



#### I. Morphological Classification

Micronodular, Macronodular, Mixed cirrhosis (size of nodules)

- II. Aetiological Classification
- 1. Viral (B, C or B with D)
- 2. Autoimmune hepatitis
- 3. Alcoholic/NAFLD
- 4. Drugs & Toxins
- 5. Biliary (Chronic Cholestatic liver disease)
- 6. Metabolic
  - a. Hemochromatosis b.Wilson's disease  $c.\alpha1$  antitrypsin deficiency
- 7. Cryptogenic (unknown) (now known as burned out NASH)

  GIT & Metabolism

#### **Classification of Cirrhosis**

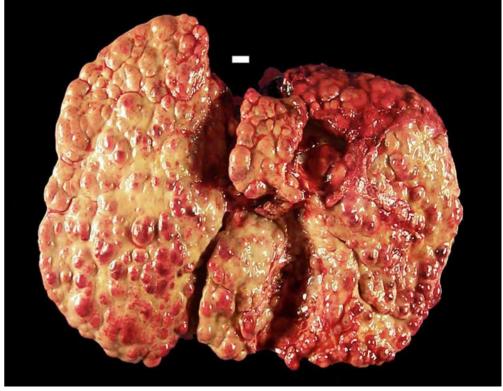




https://library.med.utah.edu/WebPath/jpeg4/LIVER011.jpg

#### **Micronodular Cirrhosis**

• Each nodule measures less than 3 mm in



https://3.imimg.com/data3/TP/XL/MY-2297891/hydatid-cysts-of-the-liver-125x125.jpg

#### **Macronodular Cirrhosis**

Each nodule measuresmore than 3mm in

al: a :aa a <del>L</del> a :a

#### Clinical picture of cirrhosis



#### **Symptoms**

- Fatigue
- Yellow discoloration in the skin and eyes (jaundice)
- Leg swelling (edema)
- Abdominal swelling (ascites)
- Bleeding or bruising tendancy

# **Symptoms**



- Itchy skin
- Spiderlike blood vessels on your skin
- Redness in the palms of the hands
- Loss of appetite
- Nausea
- Weight loss

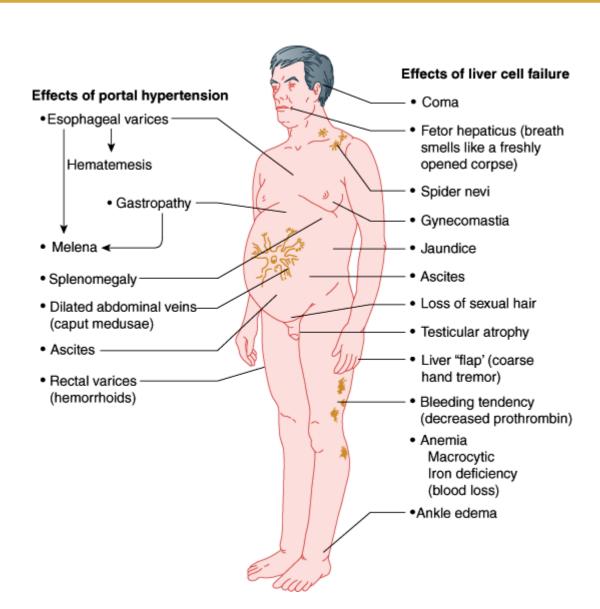
## **Symptoms**



- For women, absence of menstruation
- For men, breast enlargement (gynecomastia) or testicular atrophy with loss of libido
- Disturbed consciousness (hepatic encephalopathy)

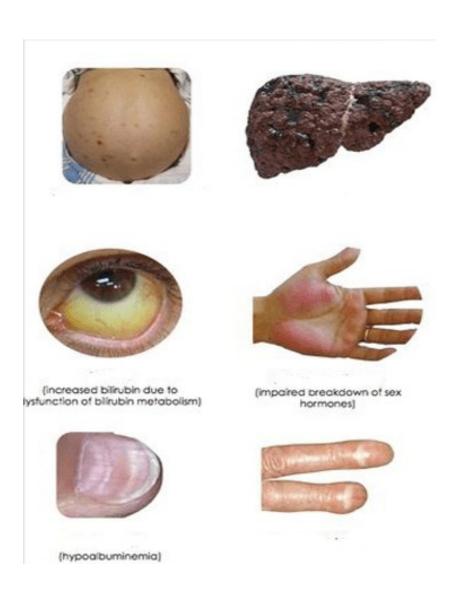
# Signs of Liver Disease





# Signs of Liver Disease





# Signs of Liver Disease





(dilated veins around the umbilicus due to portal htn)



(impaired breakdown of estrogens)



(isolated telangiectosias)



(defective coagulation)



(abnormal motor fct due to



(characteristic odor due to volatile gramatic compounds

# **Investigating Liver Disease**



Tissue	Imaging and Interventions	Laboratory
Liver Biopsy	Ultrasound	Liver Enzymes (ALT,AST,ALP,GGT)
	CT (Triphasic)	Liver Functions (Albumin, Bilirubin, INR)
	MRI	Viral Markers (HCV-Ab, HBsAg, PCR)
	MRCP	Autoimmune Markers (ANA, ASMA, IgG, AMA, ANCA)
	ERCP	Complete Blood Count
	Endoscopy	<b>Kidney Functions</b>
		Others (A1AT, Copper,



1.Portal hypertension

2. Hypoalbuminia

3.Impaired clotting factor synthesis

4. Failure of inactivation of estrogen >>?

5.Liver cell failure

6.Hepatocellular carcinoma (HCC)

# Complications of Cirrhosis ?What is Portal Hypertension-1



**Def:** Increase of portal pressure>5-10 mmHg

#### **Pathogenesis:**

- Increased resistance to flow at sinusoidal level &
   CV
- 2. Compression of portal vein radicles & CV by regenerating nodules
- 3. Anastomosis between arterial & portal systems in

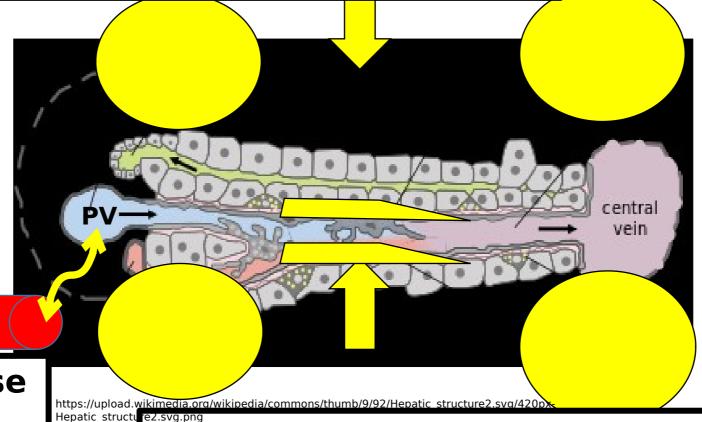
the fibrage bands > Dorte evetemis shout

# **Pathogenesis of Portal Hypertension**



(1)Increased resistance to flow at sinusoidal level & CV

https://www.youtube.com/watch?v=Cox6Z5pqMBo



3.Shunt impose arterial pressure on nortal V

HA

(2)compression of portal vein radicles & CV by regenerating nodules

# Complications of Cirrhosis Effects of Portal Hypertension-1



#### a. Ascites



https://www.homeremedyhacks.com/wp-content/uploads/2017/07/ascites-696x536.jpg

# b. Spleenomegaly&hypersplenism>>Pan

cyto



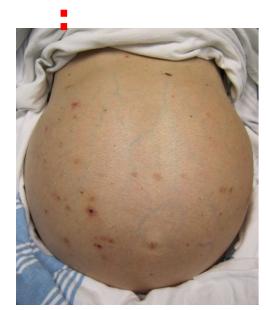
https://image.slidesharecdn.com/6stevekornblau-150518171041-lva1-app6891/95/treatment-of-high-risk-myelofibrosis-20-638.jpg?cb=1431969714

# Complications of Cirrhosis Effects of Portal Hypertension-1

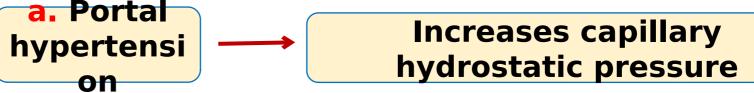


**a. Ascites** Def: Collection of excess fluid in the peritoneal cavity.

**Pathogenesis** 



https://upload.wikimedia.org/ wikipedia/commons/a/a3/ Hepaticfailure.jpg





Hyperaldoster onism

Salt & water retention

# Complications of Cirrhosis Effects of Portal Hypertension-1

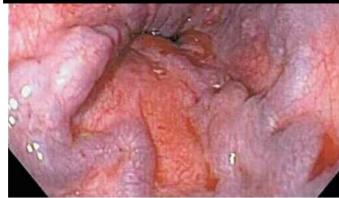


c.Portosystemic shunts

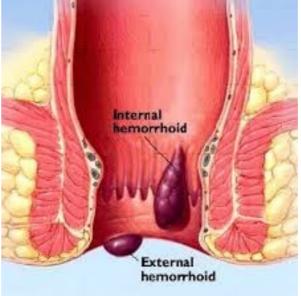
# INTERNAL ESOPHAGEAL

#### MOST DANGEROUS IN PH

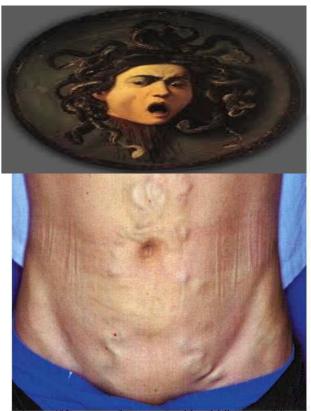
>>>Hematemesi



https://accessmedicine.mhmedical.com/data/books/2129/



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https://i0.wp.com/images-prod.healthline.com/hlcmsresou topic\_centers/4174-Caput\_Medusae\_642x361.jpg?w=115!

https://i.ytimg.com/vi/Cox6Z5pqMBo/maxresdefault.jp

#### **Esophageal varices**

#### **Piles**



2. Hypoalbuminemia: edema & <u>ascites</u>

3.Impaired clotting factor synthesis & hypersplenism: bleeding > (Prothrombin Time prolonged)

- 4. Failure of inactivation of oestrogen:
- Testicular atrophy & gynecomastia in males









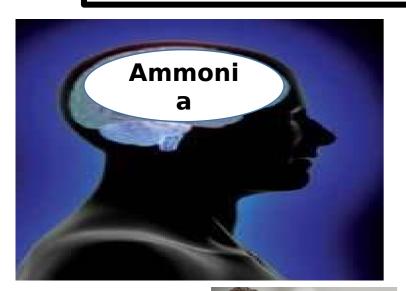
https://integrityskin.com.au/wpcontent/uploads/2016/02/Integrity-Paramedical-Skin-Practitioners-Brisbane-Laser-Clinic-Spider-

http://medicalpoint.org/ wp-content/uploads/ 2016/01/palmar-



#### **5.Liver cell failure**

**Hepatic encephalopathy &** multiple organ failure(resp/renal)



Severe loss of hepatocellular function

**Non detoxified Ammonia** 

**Affects brain** 





**epatic encephalopathy** 

Neuropsychiatric disturbances (apathy, disorientation, tremors & finally coma) with liver dysfunction

https://media.istockphoto.com/photos/confused-elderly-man-with-remote-control-picture-id537599991?



#### **6.Hepatocellular Carcinoma**



https://www.pharmaceutical-technology.com/wp-content/uploads/sites/10/2018/06/Hepatocellular\_carcinoma\_1.jpg

# **Complications of Cirrhosis (summary)**



**Esophageal** 

Caput medusa

varices

Piles

- 1. Portal hypertension leading to
  - Ascites b. Splenomegaly>hypersplenism
  - c.Portosystemic shunts
- 2. Oedema & ascites( hypoprotenemia &PH
- 3. Bleeding tendency (dt hyperspleenism &
- 4. Failure of inactivation of oestrogen>>
  - testicular atrophy & hyperplasia of breast in males
  - (gynaecomastia) & amenorrhea in females
  - Spider nevi Palmar erythema

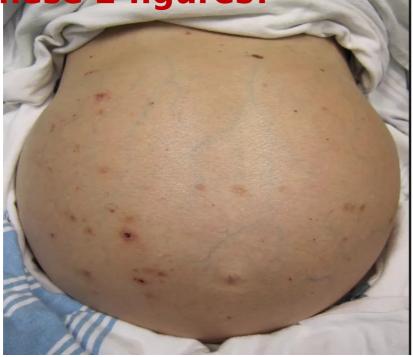
- 5. Hepatic failure & encephaopathy
- 6. Hepatocellular carcinoma

# **Complications of Cirrhosis (Quiz)**



What are the effects/Complications of cirrhosis present

in these 2 figures?



Ascites & beacking wikipedia/commons/a/a3/



Spleenomegal

http://tisus.com/resources/library/teaching-files/spleen/355875.jpg

## Complications of Cirrhosis (Quiz )





## Give reasons: Ascites occurs in liver cirrhosis

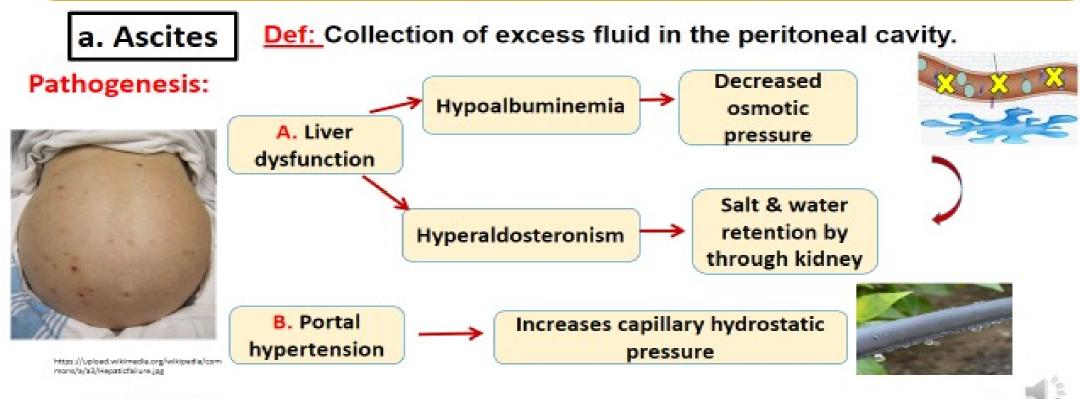
## **Complications of Cirrhosis (Quiz)**



## Give reasons: Ascites occurs in liver cirrhosis

OII & 1 10 CO DO 110111





Friday, October 23, 2020

## Effects of cirrhosis on blood tests (Quiz)



# State whether these tests are high or low in liver cirrenceing inases (AST, ALT)

**Platelet count** 

**WBC** count

**Biluribin** 

**Alkaline phosphatase** 

**RBC** count

**Prothrombin time** 

## Effects of cirrhosis on blood tests (Quiz)



## State whether these tests are high or low in liver cirrensgipinases (AST,ALT) H

Platelet count

WBC count

**Biluribin** H

Alkaline phosphatase H

RBC count

Prothrombin time H

## **Keypoints**



- Cirrhosis is conversion of normal hepatic architecture into structurally abnormal nodules by fibrosis
- •
- Pathogenesis of cirrhosis involves activation of Ito cells that are responsible for collagen deposition
- Effects & Complications of cirrhosis
- Pathogenesis of Portal Hypertension
- Pathogenesis of ascites

#### Prevention



- Do not drink alcohol if you have cirrhosis. If you have liver disease, you should avoid alcohol.
- Eat a healthy diet. Choose a plant-based diet that's full of fruits and vegetables. Select whole grains and lean sources of protein. Reduce the amount of fatty and fried foods you eat.

#### Prevention



- Maintain a healthy weight to avoid fatty liver.
- Avoid high risk behaviors like sharing needles and having unprotected sex.
- Hepatitis B vaccination.

#### Treatment of Liver Cirrhosis



- Specific therapies according to cause:
- Prednisone and azathioprine For autoimmune hepatitis
- Antiviral agents For hepatitis B and C

#### Treatment of Liver Cirrhosis



#### Specific therapies according to cause:

- Phlebotomy For hemochromatosis
- Ursodeoxycholic acid For primary biliary cirrhosis
- Trientine and zinc For Wilson disease
- Once cirrhosis develops, treatment is aimed at the management of complications as they arise.

### Ascites



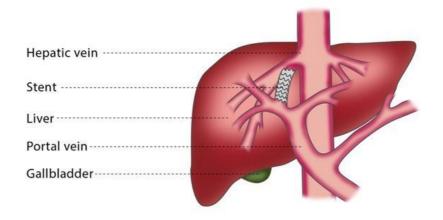
- Ascites
- Sodium restriction
- Diuretics
- Large-volume paracentesis
- Shunts

### Variceal Bleeding



- Injection sclerotherapy of gastric varices
- Endoscopic band ligation of esophageal varices
- TIPS procedure if failed previous measures

#### Transjugular intrahepatic portosystemic shunt (TIPS)



## **Hepatic Encephalopathy**



- Hepatic encephalopathy
- Lactulose
- Antibiotics

## **Liver Transplantation**



 Patients should be referred for liver transplantation if hepatic decompensation starts.

## References



- Andreoli and Carpenter's Cecil Essentials of Medicine (8ty edition)
- Toronto Notes 2017

#### **Suggested Textbooks**



Neil D. Theise. Liver and gall bladder. In Robbins and Cotran

pathologic basis of disease, 10<sup>th</sup> edition. Kumar, Abbas &

Aster (eds). Elsevier Saunders. Pages 637-676



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